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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/442,111	11/17/1999	SHAWN DEFREES	14137-01382O	5434

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/442,111	DEFREES ET AL.	
	Examiner	Art Unit	
	CHRISTIAN L. FRONDA	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53,55-57,61,66-68,73 and 74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53,55-57,61,66-68,73 and 74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 53, 55-57, 61, 66-68, 73, and 74 are pending and under consideration in this Office Action.

2. The rejection of claims 53, 55-57, 61, 66-68, 73, and 74 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in view of applicants' arguments and significant amendments to the claims in the amendment filed 12/12/2007.

3. The rejections of claims 53, 55-57, 61, 66-68, 73, and 74 under 35 U.S.C. 103(a) stated in the previous Office Actions have been withdrawn in view of significant amendments to the claims in the amendment filed 04/12/2007.

Claim Rejections - 35 U.S.C. § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

According to MPEP 2143:

> "Exemplary rationales that may support a conclusion of obviousness include:
>
> (A) Combining prior art elements according to known methods to yield predictable results;
>
> (B) Simple substitution of one known element for another to obtain predictable results;
>
> (C) Use of known technique to improve similar devices (methods, or products) in the same way;
>
> (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results;
>
> (E) " Obvious to try " – choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;
>
> (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art;

(G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention.

Note that the list of rationales provided is not intended to be an all-inclusive list. Other rationales to support a conclusion of obviousness may be relied upon by Office personnel."

5. Claims 53, 55-57, 66-68, 73, and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kittelmann et al. (Appl Microbiol Biotechnol. 1995 Dec;44(1-2):59-67; PTO 892) in view of WO 96/32491 (published 10/17/1996; PTO 892), Gilbert et al. (Eur J Biochem. 1997 Oct 1;249(1):187-94; PTO 892), and Fujio et al. (Biosci Biotechnol Biochem. 1997 May;61(5):840-5; reference of record).

Kittelmann et al. teach a method comprising culturing *E. coli* host cells expressing CMP-sialic acid synthetase to produce CMP-neuraminic acid. See entire publication especially pages 61-66. The teachings of the reference differ from the claims in that a heterologous CMP-sialic acid synthetase is not used.

WO 96/32491 teaches CMP-sialic acid synthetase that are heterologous to *E. coli* and use of the enzyme in the synthesis of CMP-sialic acid. See entire publication especially pages 8-10.

Gilbert et al. teach a recombinant *Neisseria meningitidis* alpha-2,3-sialyltransferase and its encoding polynucleotide. See entire publication especially pages 189-193.

Fujio et al. teach high level expression of XMP amidase in *E. coil* host cell transformed with a polynucleotide encoding XMP amidase, permeabilization of the *E. coil* host cell with xylene, and addition of exogenous nucleotides to the permeabilized *E. coil* host cell for the production of 5'-guanylic acid (see entire publication).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Kittelmann et al. such that the *E.coli* cells are transformed with nucleic acids encoding the CMP-sialic acid synthetase that are heterologous to *E. coli* taught by WO 96/32491 and *Neisseria meningitidis* alpha-2,3-sialyltransferase taught by Gilbert et al., the transformed *E.coli* cells permeabilized with 1% xylene taught by Fujio et al., and the permeabilized *E.coli* cells contacted with the acceptor saccharide lactose. One of ordinary skill in the art at the time the invention was made would detect and isolate the product saccharide for the purposes of quantifying and determining the purity of the product saccharide.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this for the purposes of having an *E.coli* host cells that can overproduce sialyllactose. One of ordinary skill in the art at the time the invention was made would have been motivated to permeabilize the *E. coli* cells with xylene in order for exogenous saccharides to be accessible to the enzymes that are in the *E. coli* cells for production of the product

sialyllactose. In regard to claims 67 and 68, it would have been obvious to inactivate genes encoding glycosyltransferases that use the produced sialyllactose for other metabolites or other polysaccharides since such inactivation would facilitate the accumulation of the product sialyllactose. Thus, the claims are within the ordinary skill in the art to make and use at the time the invention was made, and was as a whole clearly *prima facie* obvious

6. Claim 61 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kittelmann et al. in view of WO 96/32491, Gilbert et al., and Fujio et al., as applied to the claims above, and further in view of Bulow et al. (Trends Biotechnol. 1991 Jul;9(7):226-31; reference of record).

The teachings of Kittelmann et al., WO 96/32491, Gilbert et al., and Fujio et al., have been stated above.

Bulow et al. teach the value of artificial bi-functional enzymes and multienzyme systems obtained by gene fusion in that such enzymes have a great potential in enzyme technology as they facilitate easy purification and favorable enzyme kinetics (see entire publication)

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the above modified method of Kittelmann et al. such that the heterologous CMP-sialic acid synthetase and α2,3-sialyltransferase are expressed as a fusion protein in order to obtain favorable enzyme kinetics such that the nucleotide sugars is generated *in situ* and can be immediately used in the production of the product saccharide

Conclusion

7. No claim is allowed.

8. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on (571)272-0934. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

10. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000. CLF

/Tekchand Saidha/
Primary Examiner, Art Unit 1652